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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,189	09/15/2005	Dirk Andre Richard Vanden Berghe	5100-000012/US	1535

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,189	VANDEN BERGHE, DIRK ANDRE RICHARD	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 October 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 10/09/08 are acknowledged.

2. Claims 12-14 and 18-20 were cancelled.

3. Claims 1 and 11 were amended.

4. Claims 1-11 and 15-17 are included in the prosecution.

Drawings

5. Applicant's separate submission of drawings on 10/09/08 is acknowledged.

Specification

6. Applicant's submission of the substitute specification on 10/09/08 is acknowledged.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-4, 6-11 and 15-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Vanden Berghe (EP 1 110 909 A1) in view of Bronder (US 5,922,360).

The claimed invention is a method for the preparation of a silicic acid including extrudate comprising forming stabilized silicic acid, by hydrolysing a silicon compound into orthosilicic acid and/or oligomers in the presence of a stabilizing agent, which is a

quaternary ammonium compound, or an amino-acid, or an amino acid source or combinations thereof; mixing the stabilized silicic acid with a carrier in an amount up to the loading capacity of the carrier for silicic acid; and extruding the resulting mixture thereby forming the extrudate.

Vanden Berghe teaches a method for preparing ortho silicic acid where an acid hydrolysable silicon compound is hydrolysed in an acid solution in the presence of a solvent agent (Page 2, [0003]). "The formed ortho silicic acid stabilized by the solvent agent, may be stabilized further by contacting the ortho silicic acid with a particulate carrier" (Page 2, [0008]). The solid carrier or combination of carriers include cellulose or derivatives such as microcrystalline cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, carboxymethylcellulose, cellulose gum, pectin, alginates, sugars or sugar alcohols, lactose, peptides and polypeptides, starch and derivatives (Page 4, [0015]). Example B discloses 65% of carrier (microcrystalline cellulose) that is mixed with 35% of a combination of concentrated ortho silicic acid with solvent (glycerol). Demineralized water is added during continuous mixing to obtain an appropriate quality of the granulated material. The plastic mass is extruded. The extruded strands are spheronized. The resulting pellets are dried to a final water content of lower than 5 %. Typical pellet size is between 800 and 1200 μm (Page 4, [0019]).

Vanden Berghe does not expressly teach the stabilization of orthosilicic acid with a quaternary ammonium compound such as choline chloride.

Bronder teaches a method for preparing a stabilized orthosilicic acid preparation which comprises: i) providing a solution containing a stabilizing agent; ii) dissolving an

inorganic silicon compound in the solution containing the stabilizing agent; and iii) hydrolyzing the silicon compound to ortho silicic acid (Col. 1, lines 39-45). Quaternary ammonium compounds are disclosed as stabilizing agents, especially choline which "has been found very suitable, which is further recommended in that it provides the option of the stabilizing agent also forming the solution for the ortho silicic acid, and an inert solvent can therefore be omitted. Another or additional type of stabilizing agent is an amino acid, such as proline or serine" (Col. 1, line 59 to Col. 2, line 6). Bronder teaches that choline may be converted to choline hydrochloride (Col. 2, lines 18-19). Bronder discloses preparations with "3-5% by weight of silicon, 70% by weight of choline hydrochloride and the rest water" (Col. 2, lines 47-51). Formulation example A discloses 3% by weight silicon in the form of ortho silicic acid, 70% by weight choline hydrochloride, the rest water (Col. 3, lines 47-49).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of stabilizing ortho silicic acid with a solvent agent and further using a carrier such as microcrystalline cellulose with the ortho silicic acid to extrude, spheronized and dry the resultant pellets, as taught by Vanden Berghe, substitute the solvent with a stabilizer such as a quaternary ammonium compound like choline or an amino acid, as taught by Bronder, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Bronder teaches that "if ortho silicic acid is formed in the presence of a stabilizing agent, polycondensation is inhibited and even avoided and, furthermore organic silicon compounds substantially do not occur" (Col. 1, lines 31-35).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of the method of preparing a silicic acid extrudate comprising the step of forming a stabilized silicic acid would have been obvious over the method of preparing a silicic acid extrudate, as taught by Vanden Berghe (Page 4, [0019]). The limitation of stabilizing silicic acid in the presence of a stabilizing agent which is a quaternary ammonium compound or an amino acid would have been obvious over the quaternary ammonium compound choline and amino acids proline or serine used to stabilize ortho silicic acid, as taught by Bronder (Col. 1, line 59 to Col. 2, line 6). The limitation of mixing the stabilized silicic acid with a carrier would have been obvious over the particulate carrier including cellulose or derivatives such as microcrystalline cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, carboxymethylcellulose, cellulose gum, pectin, alginates, sugars or sugar alcohols, lactose, peptides and polypeptides, starch and derivatives, as taught by Vanden Berghe (Page 2, [0008] and Page 4, [0015]). The limitation of extruding the mixture would have been obvious over the extrusion of the mixture, as taught by Vanden Berghe (Page 4, [0019]).

Regarding instant claim 2, the limitation of orthosilicic acid would have been obvious over the orthosilicic acid taught by Vanden Berghe (Page 2, [0008]).

Regarding instant claims 3 and 15, the limitation of choline chloride as the quaternary ammonium compound would have been obvious over the choline hydrochloride taught by Bronder (Col. 2, lines 1-4).

Regarding instant claims 4 and 16, the limitation of the amino acids such as proline and serine would have been obvious over the amino acid stabilizers such as proline and serine taught by Bronder (Col. 2, lines 5-6).

Regarding instant claim 6, the limitation of 2.5-3.5% by volume silicon, 65-75% by weight choline, and 15-25% by weight water would have been obvious over formulation example A that discloses 3% by weight silicon in the form of ortho silicic acid, 70% by weight choline hydrochloride, the rest water, as taught by Bronder (Col. 3, lines 47-49).

Regarding instant claim 7, the limitation of the carrier mixed with the stabilized silicic acid in a ratio of 65-50% and 35-50% respectively would have been obvious over 65% of carrier (microcrystalline cellulose) that is mixed with 35% of a combination of concentrated ortho silicic acid with solvent (glycerol) as taught by Vanden Berghe (Page 4, [0019]) in view of the silicic acid stabilized with choline as taught by Bronder (Col. 2, lines 1-4).

Regarding instant claim 8, the carrier would have been obvious over the particulate carrier including cellulose or derivatives such as microcrystalline cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, carboxymethylcellulose, cellulose gum, pectin, alginates, sugars or sugar alcohols, lactose, peptides and

polypeptides, starch and derivatives, as taught by Vanden Berghe (Page 2, [0008] and Page 4, [0015]).

Regarding instant claim 9, the limitation of microcrystalline cellulose would have been obvious over the microcrystalline cellulose taught by Vanden Berghe (Page 4, [0015]). The limitation of the loading capacity for stabilized silicic acid < 50% would have been obvious over the 35% of a combination of concentrated ortho silicic acid with solvent (glycerol) as taught by Vanden Berghe (Page 4, [0019]).

Regarding instant claim 10, the limitation of spheronizing the extrudate into particles would have been obvious over spheronizing extruded strands, as taught by Vanden Berghe (Page 4, [0019]).

Regarding instant claim 11, the limitation of drying the particles and having a particles size between about 800 to about 1200 μm would have been obvious over drying the resulting pellets and the typical pellet size that is between 800 and 1200 μm, as taught by Vanden Berghe (Page 4, [0019]).

9. Claims 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vanden Berghe (EP 1 110 909 A1) in view of Bronder (US 5,922,360) and further in view of Seguin et al. (US 6,335,457).

The teachings of Vanden Berghe and Bronder are stated above.

Vanden Berghe and Bronder do not expressly teach a polypeptide or a protein hydrolysate as an amino acid source.

Seguin teaches “complexing ortho silicic acid with a polypeptide which acts as a stabilizer by forming hydrogen bonds with orthosilicic acid. This prevents the formation

of siloxane bonds and orthosilicic acid polymerisation" (Col. 2, lines 50-54). Seguin teaches that the ortho silicic acid complexed with a polypeptide shows excellent stability of the concentrated solid form, and is able remain stable during its transit in the gastrointestinal tract, and this despite the existence of different physiological pH favouring its polymerisation (Col. 2, lines 59-63). Example 1 discloses the preparation of an orthosilicic acid powder with hydrolyzed gelatin and Example 2 discloses the preparation of an orthosilicic acid powder with a wheat protein hydrolysate (Col. 3, line 60 to Col. 4, line 26).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of stabilizing ortho silicic acid with a solvent agent and further using a carrier such as microcrystalline cellulose with the ortho silicic acid to extrude, spheronized and dry the resultant pellets, as taught by Vanden Berghe, substitute the solvent with a stabilizer such as a quaternary ammonium compound like choline or an amino acid, as taught by Bronder, further combine it with complexing silicic acid and a polypeptide stabilizing agent, as taught by Seguin, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Seguin teaches that the polypeptide stabilizer forms hydrogen bonds with orthosilicic acid and this prevents the formation of siloxane bonds and orthosilicic acid polymerisation (Col. 2, lines 50-54).

Regarding instant claims 5 and 17, the limitation of polypeptide or protein hydrolysate as the amino acid source would have been obvious over the polypeptide

stabilizer (Col. 2, lines 5-6) and the hydrolyzed gelatin and wheat protein hydrolysate (Col. 3, line 60 to Col. 4, line 26) taught by Seguin.

Response to Arguments

Rejection of claims 1-4, 6-11 and 15-16 under 35 USC § 103(a)

10. Applicant's arguments, see Page 8, filed 10/09/08, with respect to the rejection of claims 1-4, 6-11 and 15-16 under 35 USC § 103(a) as being unpatentable over Vanden Berghe (EP 1 110 909 A1) in view of Bronder (US 5,922,360) have been fully considered but are not persuasive.

Applicant argues that Vanden Berghe relates to providing a solid formation of stabilized silicic acid by extrusion, and this is achieved by an "acid solvent agent" as a component to the formulation. Applicant argues that the solvent agent used in Vanden Berghe has a boiling point higher than 130°C, and is in liquid state between -10 and 40°C (par. 7 of Vanden Berghe, last sentence: "A common set of properties for all solvent agents are...'). Applicant argues that the teaching of Vanden Berghe is thus that the solvent agent should be a liquid at -10 and 40°C. Applicant argues that the resulting extrudate can be finely pelletized for further formation of dosage forms. Applicant argues that Bronder is directed to providing a liquid preparation of orthosilicic acid stabilized by a stabilizing agent and that although Bronder gives some general suggestions to provide solid preparations, these suggestions are not at all directed to an extrusion process, to obtain a solid that can be further processed. Applicant argues that Bronder only discloses mixing a solid sugar/maltose carrier in the liquid preparation, which is directly pressed into tablets (Formulation example C).

Applicant argues that in hindsight, the skilled person would not have been motivated to try using the stabilizing agent of Bronder in the method of Vanden Berghe, because the stabilizing agent of Bronder does not fulfill the criteria of boiling point and liquid state as defined for the solvent agent of Vanden Berghe. Applicant argues that all stabilizing agents disclosed in Bronder are solid compounds at room temperature, i.e., -10 and 40°C. Applicant argues that the skilled person would also recognize that such a change of a formulation would largely affect the subsequent extrusion process which is sensitive to the exact composition of a formulation that is extruded.

Applicants submit that incorporating the stabilizing agent of Bronder into the method of preparing a silicic acid by extrusion described in Vanden Berghe would change the basic operation of the method described in Vanden Berghe, which requires that the solvent agent have a boiling point higher than 130°C, and be in liquid state between -10 and 40°C.

This is not persuasive because according to Bronder, prior to stabilization with a carrier, in the hydrolysis step the stabilizer and silicic acid are in liquid form. Bronder teaches: “starting point for the preparation of the ortho silicic acid-comprising preparation is a solution containing the stabilizing agent” (Col. 2, lines 8-10). Therefore, the solvent agent of Bronder is in a solution with the ortho silicic acid, and will intrinsically be a liquid at -10 and 40ºC.

One of ordinary skill in the art would substitute the solvent of Vanden Berghe with the stabilizing choline chloride of Bronder because Bronder teaches the incorporation of the stabilizer with the silicic acid in a solution. The motivation to use the choline chloride

stabilizer is further provided by Bronder who teaches that: "if ortho silicic acid is formed in the presence of a stabilizing agent, polycondensation is inhibited and even avoided and furthermore organic silicon compounds substantially do not occur" (Col. 1, lines 31-35).

After the hydrolysis step, one of ordinary skill in the art would follow the process disclosed by Vanden Berghe which includes further stabilization of the formed, ortho silicic acid by contacting it with a particulate carrier (Page 2, [0008]), and then extrude the resulting plastic mass (Page 4, [0019]). Therefore, one of ordinary skill in the art would substitute the solvent of Vanden Berghe with the stabilizing solution of Bronder with a reasonable expectation of success in producing a functional stabilized silicic acid.

Therefore, the rejection of 06/09/08 is maintained.

Rejection of claims 5 and 17 under 35 USC § 103(a)

11. Applicant's arguments, see Page 10, filed 10/09/08, with respect to the rejection of claims 1-4, 6-11 and 15-16 under 35 USC § 103(a) as being unpatentable over Vanden Berghe (EP 1 110 909 A1) in view of Bronder (US 5,922,360) and further in view of Seguin et al. (US 6,335,457) have been fully considered but are not persuasive.

With respect to claims 5 and 17, Applicants incorporate the discussion presented above with respect to the deficiencies of Vanden Berghe and Bronder to teach or suggest the method for preparing a silicic acid as recited in claim 1.

This is not persuasive because, as discussed above, prior to stabilization with a carrier, in the hydrolysis step the stabilizer and silicic acid are in liquid form. Bronder teaches: "starting point for the preparation of the ortho silicic acid-comprising

preparation is a solution containing the stabilizing agent" (Col. 2, lines 8-10). Therefore, the solvent agent of Bronder is in a solution with the ortho silicic acid, and will intrinsically be a liquid at -10 and 40ºC. One of ordinary skill in the art would find it obvious to substitute the solvent of Vanden Berghe with the choline chloride of Bronder in solution with the silicic acid.

Therefore, the rejection of 06/09/08 is maintained.

Conclusion

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
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